# Bioengineering 143/243
# Computational Methods in Biology

An introduction to biophysical simulation methods and algorithms, including molecular dynamics, Brownian dynamics, Monte Carlo, mathematical optimization, and "non-algorithmic" computation such as neural networks. Various “case studies” in applying these methods in the areas of protein folding, protein structure prediction, ligand binding, aggregation and protein enzymatics will be covered. A team competition in methods development and prediction on lattice proteins serves as the final exam, and will utilize high performance computing facilities at NERSC.

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**Offered: Spring semester, 2007**

**Units:** 4

**Prerequisites:** Math 53 and 54. Graduate students must be able to or willing to learn to program in a scientific computing language (C, C++, Fortran) or Java.

**Workload:** 3 hours of lecture per week plus one hour of lab. Instructor will hold office hours for two hours per week. There will be one in-class exam, weekly homework, and one final exam project. The projects will involve application of learned algorithms and methods and team participation in a class competition. An organized presentation of the final project is to be presented orally and posted on the course web site.

| **Assessment:** | | |
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| | Mid-term exam: | 20% |
| | Homework: | 40% |
| | Final Project: | 40% |

**Text:** Understanding Molecular Simulation: From algorithms to applications, D. Frenkel and B. Smit (Academic Press, 1996).

**Text Resources:** Computer Simulation of Liquids, M. P. Allen and D.J. Tildesley (Oxford Univ. Press) 1997. Numerical Recipes, the Art of Scientific Computing, W. H. Press, B. P. Flannery, S. A. Teukolsky, W. T. Vetterling (Cambridge) 1989. Molecular Modelling: Principles and Applications, Andrew R. Leach, Prentice Hall.

# Syllabus:

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| **January 17, 19:** | **(1, 2) Introduction to Molecular Biology and Biophysics**<br>**Class organization, Intro to Physical Theories of Matter/Connections to Simulations, Molecular Biology Primer on Sequence, Structure, Function, Protein folding and disease, Protein-Ligand or Protein-Protein Interactions** |
| **January 22, 24:** | **(3, 4) Potential Energy Surface and Model Interations**<br>**Potential energy surface , All atom models: ab initio vs. empirical potential energy surfaces, Coarse-grained protein models: lattice and off-lattice bead models** |
| **January 26, 29:** | **(5, 6) Probability Theory**<br>**Elementary probability, Stochastic variables, Probability distribution functions, Discrete distributions: Binomial, Poisson, Random walk in 1D, 3D, Continuous distribution: Normal or Gaussian, Central limit theorem** |
| **Jan. 31, Feb. 2, 5:** | **(7, 8, 9) Introduction to Monte Carlo Methods**<br>**Monte Carlo Integration, Importance Sampling, Markov chain; Detailed balance, Metropolis Monte Carlo, Illustrated for atomic clusters and for chain molecules**<br>**Lattice protein folding** |
| **Feb. 7, 9, 12, 14, 16:** | **(10, 11, 12, 13, 14) Introduction to Molecular Dynamics**<br>**Time vs. ensemble average, Symplectic properties and stable numerical trajectories, Numerical integration scheme: Verlet, Velocity Verlet, Beeman, Predictor-Corrector, Velocity assignment: Box Mueller, Temperature, Truncation schemes and corrections, Neighbor Lists**<br>**Liquid water and hydrophobic effect** |
| **Feb. 21, 23, 26, 28:** | **(15, 16, 17, 18) Introduction to Optimization**<br>**Mathematical optimization: definitions**<br>**Local optimization: Golden Section; bracketing minima, Steepest descent, Conjugate gradients, Newton Method, BFGS**<br>**Global optimization: Simulated Annealing, Dynamic programming, Branch and Bound**<br>**Lennard-Jones clusters** |
| **March 2, 5, 7, 9:** | **(19, 20, 21, 22) Biology Inspired Computing**<br>**Genetic Algorithms, Neural Networks, DNA Computing**<br>**Protein structure prediction** |
| **March 12, 14, 16:** | **(23, 24, 25) Free Energy Simulation Methods** |

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| | **Widom insertion / deletion, Umbrella sampling, Thermodynamic integration, Acceptance ratio methods**<br>**Protein-ligand binding** |
| **March 19, 21, 23:** | **Mid-Term exam review**<br>**In class exam**<br>**(26) Class Competition in Simulation and Prediction** |
| **March 26-30:** | **Spring Break** |
| **April 2, 4, 6:** | **(27, 28, 29) Coarse-Grained Simulation Methods**<br>**Langevin equation , Brownian Dyanmics, Multipole expansions Debye-Huckel, Hydrodynamic Interactions**<br>**Protein enzymatics** |
| **April 9, 11, 13, 16, 18:** | **(30, 31, 32, 33, 34) Advanced Monte Carlo Methods**<br>**Microcanonical, canonical, and other ensembles, Hybrid Monte Carlo/Molecular Dynamics, Smart Monte Carlo: Force Bias, Configurational-bias Monte Carlo, Lattice chains, Flexible chains, Stiff chains**<br>**Protein aggregation** |
| **April 20, 23, 25, 27, 30:** | **(35, 36, 37, 38, 39) Advanced Molecular Dynamics Methods**<br>**Stochastic and Extended System methods, Algorithms for Dynamics in NVT and NPT ensembles: Nose-Hoover thermostats and barostats, Multiple time step approaches, Constraint dynamics, Ewald methods** |
| **May 2, 4, 7:** | **(40, 41) Simulation Methods of the Future**<br>**Quantum Chemistry and Ab initio MD, MultiScale Models** |
| **May 8:** | **Written reports due in lab** |
| **Final Exam (Oral):** | **Competition Results and Presentation by Group Leaders** |